Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

believe to be generalisable study results across England, limitations of this study include the lack of some explanatory factors that are not routinely well captured in existing data sources, such as occupation. Further work is required to understand why these differences have occurred, and in other settings.

The pressing challenge is now ensuring that COVID-19 vaccination programmes are rolled out effectively in all minority ethnic groups. Key to this will be ensuring that the need for increased vaccine confidence is urgently addressed. There are reports of increased hesitancy among minority ethnic groups, including those working in front-line health and social care roles, who are known to face an increased risk of COVID-19.[6–8] Unless direct measures are taken to increase vaccine confidence, differential vaccine uptake could further exacerbate health inequalities faced by minority ethnic groups compared with White groups.

The value of being able to analyse routinely collected health data at scale to support the rapid implementation of public health and medicine regulatory recommendations using secure data platforms has been proven during the pandemic.[9,10] An ongoing issue remains the lack of adequate mandatory ethnic coding in National Health Service (NHS) medical records, compounding the difficulty in identifying the actual scale of health inequalities. A key recommendation, which is in line with those made by health experts and Public Health England, should therefore be to comprehensively mandate the collection and recording of ethnicity data routinely within NHS and social care data collection systems.[4,11] Mathur and colleagues' findings clearly demonstrate the public health importance of not only collecting such data, but also making it accessible for analysis.

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Population immunity and vaccine protection against infection

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Vaccines act by two broad main mechanisms. They can block infection occurring entirely or they can halt the progression to symptoms after infection occurs.[1] The most direct pathway to population immunity is the first mechanism, also known as sterilising immunity. Because, if a person cannot get infected, they cannot transmit. For this reason, there has been tremendous interest in determining the extent to which COVID-19 vaccines block infection. By now, it is clear that the vaccines are remarkably effective against severe disease and some tantalising preliminary findings have suggested substantial protection against infection.[2–4] However, studies to date have mostly been from relatively small subgroups in trials, are ecological in design, or used proxies for asymptomatic infection rather than directly swabbing and testing individuals.

In December, 2020, the BNT162b2 mRNA (Pfizer–BioNTech) and ChAdOx1 nCOV-19 adenoviral (Oxford–AstraZeneca) vaccines received emergency use authorisation in the UK based on safety and efficacy data

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from clinical trials.[5,6] Both trials reported high efficacy against symptomatic COVID-19, but protection against SARS-CoV-2 infection was not reported.

In *The Lancet*, Victoria J Hall and colleagues[7] report the effectiveness of BNT162b2 against SARS-CoV-2 infection from the observational SIREN (SARS-CoV-2 Immunity and REinfection EvaluatioN) study, a rigorous, prospective, longitudinal cohort study of 23 324 health-care workers (HCWs) in hospitals in England. Most participants were female (84%), of white (88%) or Asian (7%) ethnicity, and in a patient-facing role (86%), with a median age of 46·1 years (IQR 36·0–54·1). The SIREN study was originally designed to assess the effect of previous SARS-CoV-2 infection against reinfection.[8] Participants regularly reported symptoms and underwent swabbing with PCR testing every 14 days and monthly serology, regardless of symptoms. When COVID-19 vaccines were rolled out in the UK and HCWs were prioritised, the SIREN study provided a platform to rapidly assess effectiveness against SARS-CoV-2 infection and COVID-19 disease by linking to electronic vaccination and test result records in addition to self-report questionnaires.

Hall and colleagues report that BNT162b2's effectiveness against asymptomatic or symptomatic infection was 70% (95% CI 55–85) 21 days after a single dose and 85% (74–96) 7 days after two doses in SIREN. With the intense surveillance protocol, the risk of missing an asymptomatic infection was small. Therefore, SIREN provides robust real-world estimates of vaccine protection against infection, a crucial component to understanding how vaccination can curtail transmission.

These results will help public health experts and policy makers to refine targets for achieving the level of population immunity through vaccination that would be needed to stop widespread transmission. Although the precise value and even the possibility of herd immunity to SARS-CoV-2 is debatable, most epidemiologists think the threshold is about 70% protected by vaccination or previous infection. To achieve that in the absence of naturally acquired immunity, nearly 100% of the population would need to be vaccinated with one dose or about 80% with two doses (based on an effectiveness against infection of 70% and 85%, respectively, from SIREN). Accordingly, a one-dose strategy might be best for averting the most deaths, but higher population immunity to quell transmission will require a full course of two doses. Reduction of transmission by vaccination for population immunity will mandate high coverage rates in the entire population, independent of age, sex, or ethnicity differences.

There are two more insights from SIREN with implications for population immunity. First, of vaccinated participants who were infected with SARS-CoV-2, 40% reported typical COVID-19 symptoms compared with 63% in the unvaccinated group. In other words, vaccinees were less likely to progress to symptoms once infected, which is the second mechanism of vaccine protection. Presence of symptoms has a complex relationship with SARS-CoV-2 transmission, since asymptomatically infected people play a key role in spread.[9] However, since breakthrough cases among vaccinated individuals shed virus at lower levels, they are probably less infectious than unvaccinated individuals are.[3] Second, in this study population, participants who previously had COVID-19 were less likely to be vaccinated. But this positive cohort still had 90% (95% CI 88–92) protection against subsequent infection, independent of vaccination, which is similar to findings from a large study in Denmark.[10] Current guidelines call for previously infected individuals to be vaccinated and we do not advocate for a change to that policy. But, if previously infected individuals have high levels of immunity while previously uninfected individuals are prioritised to be vaccinated, the vaccination programme will be more efficient at achieving population immunity than one immunising the population at random.

In summary, the results from the SIREN study represent a big, encouraging step forward in our understanding that BNT162b2—and most likely other COVID-19 vaccines—provide substantial protection against infection. In addition to directly protecting vaccinated individuals, COVID-19 vaccines provide a safe way of getting community transmission under control.

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Cagrilintide plus semaglutide for obesity management

Despite the huge prevalence of obesity worldwide, approved pharmacological treatment options are scarce and do not satisfactorily bridge the gap in efficacy between lifestyle behavioural changes and bariatric surgery to attain sustained long-term results.[1] Combination therapy in diabetes and hypertension treatment is commonplace in most high-income countries;[2,3] however, in obesity few options are generally available. Interestingly, some of the most promising anti-obesity candidates for dual therapy are co-agonists of the gut hormones GLP-1, glucagon, amylin, and gastric inhibitory peptide.[4]

In *The Lancet*, Lone Enebo and colleagues[5] report their 20-week randomised phase 1b trial, completed at a single centre in the USA, investigating the safety, tolerability, pharmacokinetics, and pharmacodynamics of once-weekly subcutaneous concomitant administration of one of six multiple-ascending doses of cagrilintide (range 0·16–4·5 mg; n=11–12 per group) or placebo (n=24), both with semaglutide (at the fixed dose of 2·4 mg). 95 participants were exposed to treatment, of whom 56 (59%) were male, 51 (54%) were Black or African American, and 41 (43%) were White. The GLP-1 analogue semaglutide is approved for treatment in type 2 diabetes in most high-income countries and for reducing cardiovascular risk in these patients, and has been shown to induce clinically relevant weight loss in the STEP programme in people with excess weight (a body-mass index [BMI] of ≥30 kg/m² without other weight-related complications, or ≥27 kg/m² in people with at least one coexisting weight-related condition).[6,7] Cagrilintide, a long-acting acylated amylin analogue, has proven efficacy for obesity treatment in phase 2 clinical trials.[8] Amylin reportedly reduces energy intake, regulates food choices and preferences, exerts glucoregulatory effects due to its co-secretion with insulin, suppresses postprandial glucagon release, and delays gastric emptying.[9] Thus, the cagrilintide plus semaglutide combination has the potential to act additively to improve weight control. The key point with combinations is the need to be more effective than monotherapy at a reasonable price in terms of both adverse events and cost.

The good news is that Enebo and colleagues found acceptable safety and tolerability of the cagrilintide plus semaglutide combination while providing substantial weight loss in this study group.[5] Co-escalation to


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